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Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Original Paper

Identification of anticholinergic activity of drugs of the Brazilian National List of Essential Drugs

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Submitted: 26-12-2018 Resubmitted: 08-01-2019 Accepted: 17-04-2020

Peer review: blind reviewer and Marco Túlio Cintra

Abstract

Objectives: Identify drugs from the National List of Essential Medicines-Rename 2018 that have anticholinergic activity and scales of anticholinergic activity available for use in clinical practice. **Methods:** Drug utilization study, emphasizing the analysis of supply. The drugs included in Brazilian National List of Essential Drugs (BNLED) 2018 were classified according to level 3 of the chemical therapeutic anatomical classification. A literature review was performed to identify anticholinergic activity measurement scales. Anticholinergic activity of BNLED 2018 drugs was determined using the Composite anticholinergic scale. **Results:** It was identified two systematic reviews, among the 13 identified scales, Duran's Scale and Composite Anticholinergic Scale. Composite Anticholinergic Scale is the most comprehensive with 197 drugs. It was found that 14.6% of the drugs have anticholinergic activity and 69.1% are included in the basic component of the national list. Drugs with central nervous system activity constitute about 50% of the substances with anticholinergic activity, mainly comprised of antipsychotics, followed by cardiovascular system drugs, mostly represented by beta-blockers. The cumulative effect of anticholinergic activities, from several drugs prescribed concomitantly, reflects the importance of verifying prescriptions and aware health professionals of strategies to reduce this impact. **Conclusions:** To measure anticholinergic load in clinical practice, 13 scales are available. The most comprehensive scale is the Composite Anticholinergic Scale. Although medicines with anticholinergic activity are uncommon among medicines included in BNLED 2018, it is needed to provide information to prescribers due to the negative clinical outcomes attributed to cumulative anticholinergic burden.

Keywords: cholinergic antagonist, drugs, essential, aged, pharmaceutical services.

Identificação da atividade anticolinérgica dos medicamentos da Relação Nacional de Medicamentos Essenciais

Resumo

Objetivo: Identificar os medicamentos da Relação Nacional de Medicamentos Essenciais-Rename 2018 que possuem atividade anticolinérgica e as escalas de atividade anticolinérgica disponíveis para uso na prática clínica **Métodos:** Estudo de utilização de medicamentos, tipo análise da oferta. Classificou-se os medicamentos da Rename 2018 segundo o nível 3 da classificação anatômica terapêutica química. Realizou-se revisão da literatura para identificação das escalas de mensuração da atividade anticolinérgica. Determinou-se atividade anticolinérgica dos medicamentos da Rename 2018, empregando a *Composite Anticholinergic Scale*. **Resultados:** Entre as 13 escalas identificadas, a *Duran's Scale* e a *Composite anticholinergic scale* foram elaborados por meio de revisão sistemática. A *Composite anticholinergic* scale é a mais abrangente com 197 fármacos. Verificou-se que, 14,6% dos fármacos possuíam atividade anticolinérgica, 69,1% desses estão compreendidos no componente básico da assistência farmacêutica. Dos fármacos que possuem atividade anticolinérgica, cerca de 50% referem-se a fármacos de ação no sistema nervoso central, compreendendo principalmente os antipsicóticos, seguidos pelos fármacos do sistema cardiovascular, que representados em sua maioria pelos beta-bloqueadores. **Conclusão:** Para mensuração da carga anticolinérgica na prática clínica estão disponíveis 13 escalas. A escala a com maior abrangência de fármacos é a *Composite Anticholinergic Scale.* Apesar dos medicamentos com atividade anticolinérgica serem pouco frequentes entre os medicamentos incluídos na Rename 2018, é necessário disponibilizar informações aos prescritores devido os desfechos clínicos negativos atribuídos a carga anticolinérgica acumulativa.

Palavras-chave: antagonistas colinérgicos, medicamentos essenciais, idoso, assistência farmacêutica.

Introduction

Drugs that have intrinsic anticholinergic properties work by blocking the acetylcholine receptors in the central and peripheral nervous system[1-4], and are considered classic anticholinergics, such as atropine and oxybutynin[5-6]. However, there are drugs that have indirect anticholinergic activity and are not related to their primary indication, such as antidepressants and antipsychotics[6]. The use of anticholinergic drugs can cause adverse effects on the peripheral (tachycardia, flushing, urinary retention, hyperthermia, blurred vision, and constipation) and central (cognitive worsening, attention deficit, confusion, and delirium) cholinergic systems[3,4].

Medications with intrinsic or indirect anticholinergic activity are used to treat chronic and acute health conditions and are included in the pharmacotherapy of most older adults[6]. The use of these drugs in the older adult population is a special concern, due to the physiological changes related to age[7,8]. Peripheral pharmacokinetic changes may cause decreased hepatic and renal clearance, raising the drug levels in the plasma and contributing to the occurrence of adverse anticholinergic events[7]. There are also central pharmacokinetic changes, which possibly influence anticholinergic sensitivity, such as increased blood-brain barrier permeability and P-glycoprotein dysfunction, which can facilitate access of the drug to the central nervous system[9].

The use of multiple drugs with anticholinergic activity determines a cumulative anticholinergic burden[3,10]. The effects of exposure to anticholinergics are consequences of the accumulation of actions from different drugs and not just of exposure to a single drug with high anticholinergic properties[10]. A significant portion of the anticholinergic burden in the prescriptions of the older adults is related to low anticholinergic drugs[11,12]. An elevated anticholinergic burden is associated with unfavorable clinical outcomes in the older adults, with an increased chance of developing cognitive impairment, and with deficits in executive function, memory, and processing speed[13-15]. In addition, it contributes to weakness, fatigue, cognitive and psychomotor deceleration, and falls[16,17].

Many drugs prescribed for the older adults are not routinely recognized as having anticholinergic activity and, thus, the risk of cumulative anticholinergic burden is neglected[17]. However, there is still no standard for measuring anticholinergic burden. Recently, several attempts have been made to produce reliable lists to measure anticholinergic burden and, consequently, the potential to produce adverse effects[5]. These scales serve as a tool to assist in the clinical practice and it is increasingly important to systematize information about the anticholinergic burden of drugs[17].

The National List of Essential Medicines (Rename) is a guiding instrument for the professional clinical practice in Brazil, contributing to the standardization of prescriptions. In addition, it is a guiding element of medication logistic actions within the scope of the Public Health System and a basis for the organization of state and municipal lists[18]. It is known that a considerable portion of the Brazilian population has free access to medications for the treatment of chronic non-communicable diseases, through public health strategies[19]. This access to medicines considered essential is provided for by the National Medicines Policy (*Política Nacional de Medicamentos*, PNM)[18]. Therefore, this study aims to identify Rename 2018 drugs with anticholinergic activity and also the scales of anticholinergic activity available for use in the clinical practice.

Methods

A drug utilization study , of the supply analysis type, which allows knowing the quality and information about the medicines available for use in the clinical practice[20].

A literature review was carried out in order to use the most robust scale and that best assessed the correlation of exposure to anticholinergic activity and the effects on the individuals. The PubMed/Medline databases were consulted, with no defined period, using the Medical Subject Headings (MeSH) terms and descriptors: (cholinergic antagonists OR anticholinergic OR nicotinic antagonists OR muscarinic antagonists) AND (scale OR load OR burden OR exposure) AND aged. The search was then limited to the English language. The articles were selected by title and abstract. Studies were included which presented a list of scores or classification of drugs regarding their anticholinergic activity. Studies that evaluated only one pharmacological class or which used a weak methodology to evaluate information available in package inserts were excluded.

Medicines from the three components of pharmaceutical assistance: basic, strategic and specialized, listed in Rename 2018 were included in the analysis. Medications in topical, otological, and inhalation pharmaceutical forms were excluded, due to the irrelevance of the systemic effects of these formulations. The drugs were classified regarding their anticholinergic activity, according to the criteria established in the article selected in the previous stage. Then, the percentage of drugs with anticholinergic burden was determined considering the total of drugs listed in Rename 2018. The drugs were classified according to Level 3 of the Anatomical Therapeutic Chemical (ATC) Classification System. The data were recorded in an Excel® spreadsheet and the statistical analysis included determinations of frequency and proportions.

Results

The database search captured 1,353 articles. Reading the title and abstract allowed selecting 19 articles for full reading. In the reading process of the 19 selected articles, six were excluded because they did not meet the inclusion and exclusion criteria. Therefore, 13 scales of classification of anticholinergic activity were identified; their methodologies and number of drugs listed were summarized in Table 1.

The methodology used in the elaboration of the scales is diversified, including determination of serum anticholinergic activity, affinity with the muscarinic receptor, expert opinion, and previous studies and scales. The Anticholinergic Drug Scale[10], Clinician-Rated Anticholinergic Score[23], Anticholinergic Risk Scale[30], Anticholinergic Cognitive Burden Scale[4], Anticholinergic Activity Scale[25], Anticholinergic Load Scale[26], Muscarinic Acetylcholinergic Receptor Antagonist Exposure[27], Anticholinergic Effect on Cognition[29], and the Anticholinergic Impregnation Scale[28,] are based on previous studies/scales and expert opinions. In addition, the Anticholinergic Activity Scale[25], Anticholinergic Load Scale[26] and Anticholinergic Impregnation Scale[28] instruments were also based on trials of serum anticholinergic activity. The Anticholinergic Effect on Cognition[29] scale also verified the affinity with muscarinic receptors for each drug found. Two systematic reviews were identified that drew up a new classification list for anticholinergic activity: the Duran's Scale[5] and the Composite Anticholinergic Scale (CAS)[21].

Table 1. Characteristics of the studies for the elaboration of the scales for measuring anticholinergic activity.

Study	Anticholinergic scale	Participants	Method	Nº. of listed medications	Classification System
Carnahan et al., 2006 (USA) [10]	Anticholinergic Drug Scale (ADS)	Older adults living in a long-term institution	Based on previously published scales and on expert opinions	117	Score 0-3
Ancelin et al., 2006 (France) [22]	Anticholinergic Burden Classification (ABC)	Individuals > 60 years old without dementia	Based on serum anticholinergic activity determined through published studies with radio-receptor and through expert opinions	27	Score 0-3
Han et al., 2008 (USA) [23]	Clinician-Rated Anticholinergic Score (CRAS)	Men with hypertension > 65 years old	Based on a previously published scale and on expert opinions	60	Score 0-3
Rudolph et al., 2008 (USA) [30]	Anticholinergic Risk Scale (ARS)	Men ≥ 65 years old in geriatric clinics and primary care	Based on literature review and on expert opinions	49	Score 0-3
Chew et al., (USA) [24]	Serum Anticholinergic Activity (SAA)	-	Based on a trial with radio-receptors	107	Score 0, 0/+, +, ++, +++
Boustani et al., 2008 (USA) [4]	Anticholinergic Cognitive Burden (ACB) Scale	-	Based on systematic review and on expert opinions	88	Score 1-3
Ehrt et al., 2010 (Norway) [25]	Anticholinergic Activity Scale (AAS)	Patients diagnosed with Parkinson's Disease	Based on the study by Chew et al., 2008 and on expert opinions	99	Score 0-4
Sittironnarit et al., 2011 (Australia) [26]	Anticholinergic Load (ACL) Scale	Individuals > 60 years old. Three groups: healthy individuals, with mild cognitive impairment and Alzheimer's disease	Based on previously published scales and on expert opinions	49	Score 0-3
Duran et al., 2013 (Ecuador) [5]	Duran's Scale (DS)	-	Systematic review of previous scales	100	0-2
Salahudeen et al., 2015 (New Zeeland) [21]	Composite Anticholinergic Scale (CAS)	-	Systematic review of previous scales	197	Cholinergic load classified into: Low, Moderate, and High.
Klamer et al., 2016 (Belgium) [29]	Muscarinic Acetylcholinergic Receptor ANTagonist Exposure (MARANTE)	-	Based on the Duran's List drugs, on authorized sources and on expert opinions	41	Potency 0-2 and dosage (0; 0.5; 1; 1.5; 2)
Bishara et al., 2017 (United Kingdom) [29]	Anticholinergic Effect on Cognition (AEC)	-	Based on literature review and on expert opinions	122	Score 0-3 (or unable to classify)
Briet et al., 2017 (France) [28]	Anticholinergic Impregnation Scale (AIS)	Patients from a psychiatric clinic	Based on previously published scales and on expert opinions	128	Score 1-3

The scale proposed by Salahudeen and collaborators[21] was based on a systematic review of scales of anticholinergic activity, seven studies were used to elaborate the classification of drugs. 197 drugs were listed, therefore being the most comprehensive. In addition, the clinical impacts of the use of the selected anticholinergic drugs were verified through studies that show an association between exposure to anticholinergic drugs and cognitive and functional adverse effects. For these attributes, the CAS[21] scale was selected for the identification and classification of drugs with anticholinergic activity included in Rename 2018. Therefore, they were classified as low, moderate, and high anticholinergic activity. Of the 375 drugs from Rename 2018, 55 (14.6%) have anticholinergic activity as described in Table 2. It was identified that 38 (69.1%) of the drugs with anticholinergic activity are of the basic component of pharmaceutical assistance, 3 (5.4%) are of the strategic component, and 17 (30.9%) are of the specialized component. It is worth mentioning that clindamycin hydrochloride and prednisone are included in the basic and strategic components. Approximately 50% of the drugs with anticholinergic activity listed in Rename 2018 are from Group N of the ATC, drugs that act on the

nervous system, especially antipsychotics, dopaminergic agents, and antidepressants, followed by Group C drugs: drugs acting on the cardiovascular system (18%), and from Group A: alimentary tract and metabolism (7.2%).

According to the CAS scale, 42 (76.4%) of the drugs have low anticholinergic activity, 5 (9.1%) have medium anticholinergic activity, and 8 (14.5%) have high anticholinergic activity (Table 3).

Discussion

The literature review on scales for measuring anticholinergic burden demonstrated heterogeneity of methodologies used in the studies, covering trials of serum anticholinergic activity with radio-receptors, *in vitro* measure of affinity for muscarinic receptors, and lists developed by a panel of experts. The systematic reviews identified made an analysis of the studies with the different methodologies, the two reviews found were based on seven studies and differed in only one study; both highlight the

Table 2. Description of the Rename 2018 Drugs with anticholinergic activity according to the CAS[21] scale and to the ATC classification.

ATC classification	Medicine	Number of medications (%)
Group A - Alimentary tract and metabolism		
A10B - Oral medication for reducing blood glucose	Metformin hydrochloride	
A02B - Medication for peptic ulcer and gastroesophageal reflux	Ranitidine Hydrochloride	4 (7.2)
A03B - Belladonna derivatives	Atropine sulfate	
A03F - Propulsive medications	Metoclopramide hydrochloride	
Group B - Blood and hematopoietic organs		
B01A - Antithrombotic agents	Warfarin	1 (1.8)
Group C - Cardiovascular system		
C01A - Cardiac glycosides	Digoxin	
C01D - Vasodilators used in heart disease	Isosorbide dinitrate, Isosorbide mononitrate	
C02D - Drugs that act on arteriolar smooth muscles	Hydralazine	
C03C - Loop diuretics	Furosemide	10 (18.0)
C07A - Beta blockers	Atenolol, Metoprolol succinate, Metoprolol tartrate	
C08C - Selective calcium channel blocker	Nifedipin	
C09A - Angiotensin-converting enzyme inhibitors	Captopril	
Group H - Systemic hormones		
H02A - Corticosteroids for systemic use	Dexamethasone, Prednisolone Sodium phosphate, Methylprednisolone, Prednisone, Hydrocortisone sodium succinate	5 (9.0)
Group J - Systemic anti-infectives		
J01F - Macrolides and Lincosamides	Clindamycin hydrochloride	1 (1.8)
Group L - Antineoplastics and immuno-modulators		
L04A - Immuno-suppressants	Azathioprine, Cyclosporine, Methotrexate	3 (5.4)
Group N - Nervous system		
N02A - Opioids	Methadone hydrochloride, Codeine phosphate, Morphine sulfate	
N03A - Antiepileptics	Valproic acid, Carbamazepine, Clonazepam, Phenobarbital	
N04B - Dopaminergic agents	Amantadine hydrochloride, Selegiline hydrochloride, Pramipexole dihydrochloride, Entacapone, Levodopa + Carbidopa*, Bromocriptine mesylate	
N05A - Antipsychotics	Lithium carbonate, Chlorpromazine hydrochloride, Ziprasidone hydrochloride, Clozapine, Haloperidol/Haloperidol decanoate, Quetiapine hemifumarate, Olanzapine, Risperidone	28 (50.6)
N05B - Anxiolytics	Diazepam	
N05C - Hypnotics and sedatives	Midazolam	
N06A - Antidepressants	Amitriptyline hydrochloride, Bupropion hydrochloride, Clomipramine hydrochloride, Fluoxetine hydrochloride, Nortriptyline hydrochloride	
Group R - Respiratory system		
R06A - Antihistamines for systemic use	Promethazine hydrochloride, Loratadine, Dexclopheniramine	3 (5.4)

discrepancies in the scores attributed to the drugs in the different scales. Salahudeen and collaborators[21] listed a greater number of drugs and compiled studies with different methodologies, which allowed for the analysis of the association between the use of drugs with anticholinergic activity and cognitive and functional outcomes, risk of hospitalization, and mortality. The use of different methods in the elaboration allows comparing the data obtained in different studies with the production of a more robust scale, since it becomes possible to associate the individual's exposure to the drugs with anticholinergic activity and the occurrence of peripheral and central adverse effects.

The results of the Rename 2018 analysis showed that the proportion of drugs with anticholinergic activity in Rename is small. Most of the drugs identified have low anticholinergic activity and are mostly included in the basic component of pharmaceutical assistance. The basic component drugs are mainly used for the treatment of prevalent and priority problems in primary care and, consequently, the population's access to these drugs is more common. In the context of the ongoing demographic and epidemiological transition in the country, chronic non-communicable diseases that require pharmacological treatment for prolonged periods become evident, and the older adults stand out for presenting multimorbidity and for being one of the main users of medications[31,32].

Most Rename drugs identified with anticholinergic activity belong to Group N, drugs with action on the nervous system. A population-based study on the use of psychiatric drugs by older adults in the community identified that benzodiapines and antidepressants were the most used therapeutic classes. It was also verified that the medical diagnosis report for depression was the factor most strongly associated with the use of psychiatric drugs.[33] The National Survey on Access, Use and Promotion of the Rational Use of Medications (*Pesquisa Nacional sobre Acesso, Utilização e Promoção do Uso Racional de Medicamentos*, PNAUM) in

Table 3. Description of the scores of the anticholinergic activity of the drugs included in Rename 2018, according to the pharmaceutical assistance component.

Medicine	Component			Medicine	Component		
	Basic	Strategic	Special		Basic	Strategic	Special
Valproic acid (sodium valproate)	1	-	-	Digoxin	1	-	-
Atenolol	1	-	-	Isosorbide dinitrate	1	-	-
Azathioprine	-	-	1	Entacapone	-	-	1
Captopril	1	-	-	Phenobarbital	1	-	-
Carbamazepine	2	-	-	Codeine phosphate	-	-	1
Lithium carbonate	1	-	-	Prednisolone sodium phosphate	1	-	-
Cyclosporine	-	-	1	Furosemide	1	-	-
Clonazepam	1	-	-	Haloperidol/Haloperidol decanoate	2	-	-
Amantadine hydrochloride	-	-	2	Quetiapine hemifumarate	-	-	1
Amitriptyline hydrochloride	3	-	-	Levodopa + carbidopa	1	-	-
Bupropion hydrochloride	-	1	-	Loratadine	1	-	-
Clindamycin hydrochloride	1	1	-	Dexchlorpheniramine maleate	3	-	-
Clomipramine hydrochloride	3	-	-	Bromocriptine mesylate	-	-	1
Chlorpromazine hydrochloride	3	-	-	Methylprednisolone	-	-	1
Fluoxetine hydrochloride	1	-	-	Methotrexate	-	-	1
Hydralazine hydrochloride	1	-	-	Midazolam	1	-	-
Methadone hydrochloride	-	-	2	Isosorbide mononitrate	1	-	-
Metformin hydrochloride	1	-	-	Nifedipin	1	-	-
Metoclopramide hydrochloride	1	-	-	Olanzapine	-	-	2
Nortriptyline hydrochloride	3	-	-	Prednisone	1	1	-
Promethazine hydrochloride	3	-	-	Risperidone	-	-	1
Ranitidine hydrochloride	1	-	-	Metoprolol succinate	1	-	-
Selegiline hydrochloride	-	-	1	Hydrocortisone sodium succinate	1	-	-
Ziprasidone hydrochloride	-	-	1	Atropine sulfate	3	-	-
Clozapine	-	-	3	Morphine sulfate	-	-	1
Dexamethasone	1	-	-	Metoprolol tartrate	1	-	-
Diazepam	1	-	-	Warfarin	1	-	-
Pramipexole dihydrochloride	-	-	1				

Classification of anticholinergic activity according to the CAS scale[21]: 1- Low anticholinergic activity 2- Medium anticholinergic activity 3- High anticholinergic activity

Brazil demonstrated that the drugs most used by individuals with depression were fluoxetine, clonazepam, and amitriptyline.[34] Benzodiazepines and tricyclic antidepressants are considered potentially inadequate drugs for the older adults due to their profile of adverse effect[15]. That is, with regard to the safety of the drug therapy, the treatment instituted in the elderly population has not been the most adequate. There are safer therapeutic alternatives for this population; however, they are not available in the public network. In addition, other drugs frequently used by this population are risperidone, haloperidol, and lithium carbonate[34]. These findings alert to the need to think about the therapeutic specificities of the older adults in future Rename reviews.

It is known that there is an increased risk of adverse drug reactions, provided by the physiological changes of aging, making this population particularly vulnerable to the cognitive effects[7]. This occurs both due to anticholinergic sensitivity and to the easy access of the drug to the central nervous system[7,9]. A number of studies have already consistently shown that changes or abnormalities in the choline transporter, acetylcholine release, and expression of muscarinic and nicotinic receptors are associated with cognitive and peripheral effects[4].

In this sense, the cumulative anticholinergic burden from drugs gains importance in the context of polypharmacy. A PNAUM showed that, of the total older adults, 18.0% used at least five medications and that this polypharmacy was higher among the oldest individuals[32].

In assessing the comorbidities, the prevalence of polypharmacy was 60.0% among those who reported at least four diseases[32]. Older adults on polypharmacy use drugs from different pharmacological classes, including anticholinergic drugs that have a direct anticholinergic effect. In addition, drugs from other pharmacological groups, such as antidepressants and antipsychotics, have indirect anticholinergic activity and are not related to their therapeutic indication[6]. It is known that the cumulative effect of several drugs with low anticholinergic activity is more common in the older adults than the use of drugs with high activity. An assessment of the prescription of anticholinergic medications for older adults in primary care in Australia identified that 70% of the anticholinergic burden in the older adults assessed was determined by the use of medications with low anticholinergic activity[11,35]. In this study, it was noticed that the drugs with high and moderate anticholinergic activity are mostly drugs that act on the nervous system. These drugs are mainly available through the basic and specialized component.

A significant proportion of prescribers do not recognize the indirect anticholinergic activity of drugs that have this property, as well as the adverse effects of anticholinergic drugs[36]. In addition, changes in pharmacokinetics and pharmacodynamics resulting from senescence and senility must be considered when making decisions about the drugs to be prescribed. This reinforces the importance of providing information on the anticholinergic activity of the drugs, especially the basic components where drugs with low

anticholinergic activity predominate. In view of this, it is relevant to encourage the development of a scale that includes information on the drugs available in Brazil that have anticholinergic activity, far beyond those included in Rename 2018. Accurate, up-to-date, and independent information about medications qualifies the prescription process, especially with regard to specificities for the older adults. It is worth mentioning the role of the pharmacist in working together with the geriatrician to qualify this prescription process and to provide safer clinical practices for the older adults.

The publication of National Therapeutic Forms[37] is recommended to provide information on medications in national health systems. Since 2008, Brazil has systematized the National Therapeutic Form with information on Rename's medications for the purpose of guiding prescribers and health professionals, contributing to the rational use of medications. The current edition, published in 2010, does not present with the necessary emphasis the anticholinergic activity of drugs, especially for those with indirect activity. It is known that the scales for measuring anticholinergic activity are heterogeneous in relation to the drugs included and that they do not fully cover all the medications with this activity. The systematization of this information for health professionals is of great value. Thus, it is suggested that these aspects be included in the drug monographs, in the National Therapeutic Form, and that the impact due to these effects be addressed in the chapter on medications in the older adults.

The knowledge of the intensity of anticholinergic activity helps in decision making and is used to calculate the total anticholinergic burden, which is based on the sum of the anticholinergic burdens assigned to each medication in use. For this, it is necessary to carry out the pharmacological anamnesis to identify all the drugs in use and then assess the anticholinergic burden of each one, using the scales in the literature. The calculation must consider the specific score of each scale. Finally, anticholinergic burdens must be added; this will be the total anticholinergic burden. A value equal to or above 3 for the total anticholinergic burden is considered clinically relevant, being necessary to assess the risk-benefit ratio of the discontinuation or replacement of the medications[35]. The MARANTE scale considers the maintenance dose of the drugs in use; the total anticholinergic burden considered clinically relevant is equal to or greater than 2 points[27].

Considering the clinical impact of the accumulation of anticholinergic burden from drugs in older adults, it is necessary to make prescribers and other health professionals aware of the strategies to reduce this impact. Some strategies can be adopted, such as using drugs with anticholinergic activity for the shortest possible treatment time; in case of chronic treatment, choosing therapeutic alternatives with less anticholinergic activity or alternatives that, in different aspects, are more suitable for the older adults to treat the health condition in question.

One of the limitations of this study is that the literature search is restricted to Pubmed/Medline. However, as a comprehensive search was carried out, without date restrictions, it was possible to identify a greater number of scales.

Despite this limitation, the study provides data for health managers, contributing to improving the quality of health care and the management of pharmaceutical care. Another strength of the research is that it contributes with elements that can subsidize actions to promote the safe use of medications, in particular directed to the older adults, whose harmful impact of the exposure to anticholinergic medications on the functionality presents scientific evidence.

Conclusion

13 scales for measuring anticholinergic activity were identified for use in the clinical practice. Medications with anticholinergic activity are uncommon among those included in Rename. The therapeutic class of the ATC system with the highest frequency of drugs with anticholinergic activity is Group N, the nervous system, with emphasis on antipsychotics. It is necessary to increase the availability of information on drugs with anticholinergic activity, especially in the National Therapeutic Form, in order to provide safer clinical practices to the older adults. Still, it is of great value that more studies be carried out to verify the anticholinergic activity of the most used drugs in Brazil.

Conflict of interest statement

The authors declare that there are no conflicts of interest regarding this article.

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